

Differential control of muscle sympathetic outflow in single units of humans: a role for pulmonary artery baroreceptors?

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1 **Differential control of muscle sympathetic outflow in single units of**
2 **humans: a role for pulmonary artery baroreceptors?**

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14 references)

15 TO THE EDITOR: We read with interest the article by Incognito and colleagues
16 (5), published recently in the American Journal of Physiology. The paper
17 describes differential control over postganglionic single unit sympathetic fibres
18 in healthy humans.

19 It is widely reported that unloading of low-pressure vagal afferents from
20 the heart and pulmonary vasculature mediates increased muscle sympathetic
21 nerve activity (MSNA) in response to non-hypotensive LBNP (12). However,
22 an alternative explanation is that altered aortic and carotid arterial
23 hemodynamics, acting through the sinoaortic baroreceptors, stimulates
24 sympathoexcitation without a detectable change in arterial pressure (3, 11).
25 Additionally, mild LBNP elicits increased MSNA and vasoconstriction in
26 cardiac transplant patients (6). Nevertheless, many in the field attribute
27 vasoconstriction in the skeletal muscle circulation during LBNP to a low-
28 pressure 'cardiopulmonary baroreflex'.

29 The article by Incognito and co-authors presents some interesting new
30 evidence. Simultaneously occurring increases and decreases in MSNA were
31 recorded from two populations of postganglionic single units in healthy young
32 participants exposed to LBNP and rhythmic handgrip exercise. Notably, there
33 are similar findings for healthy middle-aged men (9), and heart failure patients
34 (8). In the previous studies, by Millar and co-authors (8, 9), two response
35 patterns in single-units were also observed during mild lower body positive
36 pressure. The so-called "paradoxical" single-unit responses were attributed to
37 unloading and loading of intrathoracic mechanoreceptors, which were
38 presumed to be responsible for sympathetic activation when stimulated.

39 However, these units were relatively small in number compared with those
40 having anticipated firing responses.

41 With this in mind, we highlight several important findings from studies
42 in animal preparations, which permit careful control of pressure stimuli to
43 reflexogenic areas in the heart and pulmonary vessels. For example, it is
44 established that atrial receptors exert little influence over sympathetic
45 vasoconstrictor activity (7). Furthermore, we have demonstrated that
46 responses attributed to ventricular receptors actually originate from
47 mechanosensitive receptors in the coronary arteries (1) and that reduced
48 ventricular filling has little effect on systemic vascular resistance (2). As a
49 matter of fact, we have shown that coronary artery baroreceptors function as
50 high-pressure receptors, and exert control over sympathetic nerve activity
51 similar to that originating from aortic and carotid baroreceptors (4). Thus, the
52 only receptors within the intrathoracic region with the potential to elicit
53 “paradoxical” sympathetic responses are the pulmonary vascular
54 mechanoreceptors. Moreover, we have observed differential control of
55 systemic vascular resistance in response to rising and falling pressures in the
56 pulmonary and carotid arteries (10).

57 Pulmonary artery baroreceptors may be of importance in mediating
58 sympathetic activation during exercise, as well as in hypoxic conditions (4).
59 However, a physiological role for these low-pressure baroreceptors in humans
60 has been largely overlooked. This may be due, in part, to the technical
61 difficulty of applying a discrete physiological stimulus to the pulmonary
62 arteries. Therefore, we commend the work of Incognito, Millar and colleagues

(5, 8, 9) for shedding new light on this possibility. In our view, their data represent exciting human evidence of the potential for a pulmonary baroreflex, and support a contribution of this to differential control of sympathetic outflow by low- and high-pressure baroreceptors. The challenge for those working in this area is to develop an approach that enables discrete stimuli to low- and high-pressure baroreceptors in humans, in order to further investigate differential control of MSNA.

AUTHOR CONTRIBUTIONS

JPM and MJD contributed equally.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

REFERENCES

1. **Drinkhill MJ, McMahon NC, and Hainsworth R.** Delayed sympathetic efferent responses to coronary baroreceptor unloading in anaesthetized dogs. *J Physiol* 497 (Pt 1): 261-269, 1996.
2. **Drinkhill MJ, Wright CI, and Hainsworth R.** Reflex vascular responses to independent changes in left ventricular end-diastolic and peak systolic pressures and inotropic state in anaesthetised dogs. *J Physiol* 532: 549-561, 2001.
3. **Fu Q, Shibata S, Hastings JL, Prasad A, Palmer MD, and Levine BD.** Evidence for unloading arterial baroreceptors during low levels of lower body negative pressure in humans. *Am J Physiol Heart Circ Physiol* 296: H480-488, 2009.
4. **Hainsworth R.** Cardiovascular control from cardiac and pulmonary vascular receptors. *Exp Physiol* 99: 312-319, 2014.
5. **Incognito AV, Doherty CJ, Nardone M, Lee JB, Notay K, Seed JD, and Millar PJ.** Evidence for differential control of muscle sympathetic single units during mild sympathoexcitation in young healthy humans. *Am J Physiol Heart Circ Physiol*, 2018.
6. **Jacobsen TN, Morgan BJ, Scherrer U, Vissing SF, Lange RA, Johnson N, Ring WS, Rahko PS, Hanson P, and Victor RG.** Relative contributions of cardiopulmonary and sinoaortic baroreflexes in causing sympathetic activation

95 in the human skeletal muscle circulation during orthostatic stress. *Circ Res* 73:
96 367-378, 1993.

97 7. **Karim F, Kidd C, Malpus CM, and Penna PE.** The effects of stimulation of
98 the left atrial receptors on sympathetic efferent nerve activity. *J Physiol* 227: 243-
99 260, 1972.

100 8. **Millar PJ, Murai H, and Floras JS.** Paradoxical muscle sympathetic reflex
101 activation in human heart failure. *Circulation* 131: 459-468, 2015.

102 9. **Millar PJ, Murai H, Morris BL, and Floras JS.** Microneurographic
103 evidence in healthy middle-aged humans for a sympathoexcitatory reflex
104 activated by atrial pressure. *Am J Physiol Heart Circ Physiol* 305: H931-938, 2013.

105 10. **Moore JP, Hainsworth R, and Drinkhill MJ.** Reflexes from pulmonary
106 arterial baroreceptors in dogs: interaction with carotid sinus baroreceptors. *J*
107 *Physiol* 589: 4041-4052, 2011.

108 11. **Taylor JA, Halliwill JR, Brown TE, Hayano J, and Eckberg DL.** 'Non-
109 hypotensive' hypovolaemia reduces ascending aortic dimensions in humans. *J*
110 *Physiol* 483 (Pt 1): 289-298, 1995.

111 12. **Victor RG and Mark AL.** Interaction of cardiopulmonary and carotid
112 baroreflex control of vascular resistance in humans. *J Clin Invest* 76: 1592-1598,
113 1985.

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